REPORT OF DR. ZHI Q. YAO, M.D., Ph.D.

I. BACKGROUND AND EXPERTISE

I am a medical doctor (M.D.) and a nationally recognized physician scientist (PH.D.) in the field of viral hepatitis. I have over 30 year experience in the diagnosis and treatment of various infectious diseases, and I have spent the entirety of my career focusing on medical treatment and scientific research of hepatitis C virus (HCV), hepatitis B virus (HBV), and human immunodeficiency virus (HIV). I am American Board of Internal Medicine (ABIM) certified in both Internal Medicine and Infectious Diseases. I am also certified as an American HIV Specialist by American Academy of HIV Medicine (AAHIVM). I am a faculty member (Distinguished Professor) in the Department of Internal Medicine, Division of Infectious Diseases at East Tennessee State University. I am currently serving as the Director of Center of Excellence for HIV/AIDS at Quillen College of Medicine, focusing on the management of patients with hepatitis C, hepatitis B, and/or co-infection with HIV. I also have a joint appointment as staff physician at James H. Quillen VA Medical Center, serving as the Director of Hepatitis (HCV/HBV/HIV) Program, overseeing > 3,000 Veterans chronically infected with HCV and/or HIV in states of Tennessee, Virginia, Kentucky, and North Carolina. I serve as Board of Directors for Mountain Home VA Research and Education Cooperation, and Chairman of the Subcommittee of Research Safety (SRS) at Veteran Administration (VA). I am a member of the American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA). I served as the Site Director of Multi-Center Clinical Trials for Direct Acting Antiviral (DAA) treatment of patients with chronic hepatitis C sponsored by the Gilead Science Inc. I am currently the Principal Investigator (PI) and Project Director (PD) of multiple National Institutes of Health (NIH) and VA-funded research grants, primarily on HCV and HIV studies. I am serving as an expert reviewer for National Institutes of Allergy and Infectious Diseases (NIAID) in the study section of Infection and Host Defense (IDH), focusing on reviewing HCV-related grants submitted from nationwide applicants to NIH. A true and correct copy of my curriculum vitae (CV) is attached as (***Exhibit A)***. I have been compensated in the amount of $8,000.00 for the study and review. My hourly rate for review is $200.00, my hourly rate for deposition testimony is $200.00.

In preparing this Report, I have reviewed the following documents:

1. Class Action Compliant

2. Response from TN Office of the Commissioner to Questions Raised During the Hearing (**EXHIBIT B**)

3. TDOC Chronic HCV Guidance: Recommendation for Testing, Managing, and Treating Hepatitis C (January 1, 2016) and TDOC Management of Chronic HCV Agenda and Protocol (**EXHIBIT C**)

4. Description of the TDOC Advisory Committee on HIV and Viral Hepatitis Prevention and Treatment Authority

5. Order Granting Plantiffs' Motion for Preliminary Injunction by the United State District Court Western District Washington at Seattle

6. Deposition Transcripts of Tony Parker (Exhibits 1-4), Kenneth Williams (Exhibits 1-9), Dr. Cortez Tucker (Exhibits 1-8), Dr. Kavin Johnson (Exhibit 1-6), Dr. Bernhard Dietz (Exhibits 1-5), and Dr. Keith Ivens (Exhibits 1-4).

7. Response to Plaintiffs' First Set of ROGS to Defendant Dr. Kenneth Williams

8. TDOC Hep C Pretreatment Program Final

9. Answer to Complaint by Marina Cadreche, Tony Parker, Kenneth Williams (Lorch, Pamela)

10. Supplemental Interrogatory Response of defendant Kenneth E. Williams

11. Motion to Certify Class by Russell L. Davis, Charles Graham

12. Memorandum in Support of 14 Motion to Certify Class filed by Russell L. Davis, Charles Graham

13. Declaration of Thomas H. Castelli filed by Russell L. Davis, Charles Graham

14. Response in Opposition re 14 Motion to Certify Class filed by Marina Cadreche, Tony Parker, Kenneth William

15. Reply to Response to Motion re 14 Motion to Certify by Russell L. Davis, Charles Graham

16. Memorandum Signed by Chief Judge Waverly D. Crenshaw, Jr. on 5-4-2017

17. Order Pending before the Court is Plaintiffs' Motion for Class Certification (Doc. No.14) for the reason

18. Distribution of HIV and HCV patients in TDOC Prisons 2017

19. The Guidance for Testing, Managing, and treating of Hepatitis C by the American Association for the Study of Liver Diseases (AASLD) (**EXHIBIT D**)

20. Supplemental Production of Medical Records of Plaintiff Russell Davis 1/9/2018 and Providers listed in Plaintiff Russell Davis' medical records

21. "Tennessee Inmate Asking for Hepatitis C Treatment Dies," The Tennessean, July 1, 2016.

All of my opinions are to a reasonably degree of medical certainty.

II. HEPATITIS C: AN OVERVIEW

1. **HCV is a Widespread and Serious Disease.** Hepatitis C is an infectious disease that affects the liver as well as other organ systems in human body. "Hepatitis" means inflammation of the liver. It is estimated that over 200 million people worldwide and as many as 5 million individuals in the United States (US) chronically infected with HCV and nearly 34,000 new cases occurred in 2015 [1, 2]. Of acute HCV infections, 15% to 25% typically resolved within 6 months of transmission; the remaining 75% to 85% infected individuals will become chronic infection [3]. Individuals with untreated chronic HCV infection can suffer from various symptoms including, but not limited to, fatigue, jaundice, joint pain, muscle pain, arthritis, nerve damage, depression, cognitive dysfunction, immune dysregulation, autoimmune disorder, increased heart attacks, diabetes, and cancer. Specifically, chronic hepatitis C significantly increases the risk of liver cirrhosis (20~40%), hepatocellular carcinoma (4~6%), and death [3, 4]. To date, HCV is the most common cause of liver failure or liver cancer that need transplantation in the US. More than 20,000 people in the US die each year due to liver disease caused by HCV, a death rate that is higher than that of any other infectious diseases. According to the Center of Disease Control (CDC) reports, the number of HCV-related deaths reached an all-time high in recent years, surpassing 60 other nationally reportable infectious conditions combined, making hepatitis C the number one reportable infectious disease that kills people in the US [5].

2. ***HCV is Contagious and transmissible through blood exposure.*** HCV typically spreads through blood transmission. Some modes of transmission of HCV are well documented and widely accepted; others are less well defined and require further study. It is clear that HCV is most frequently transmitted through large or repeated direct exposures to infected blood. The two most common exposures associated with transmission of HCV are blood transfusion and injection drug use. Other modes of transmission include rough sex and other unknown sources.

   Blood Transfusion/Receipt of Blood Products: HCV infection occurs when the blood of an infected person enters the body of an uninfected person. Today, HCV is rarely transmitted by blood transfusion or transplantation of organs due to thorough screening of the blood supply for the presence of the virus and inactivation procedures that destroy blood-borne viruses since 1999. In the last several years, blood banks have instituted techniques that utilize nucleic acid amplification of the HCV, which will detect the presence of virus even in newly-infected patients who are still HCV antibody-negative. These techniques are estimated to have prevented transfusion-associated HCV infections per year in the US,

and have lowered the current risk of acquiring HCV via transfused blood products to 1 in 2 million [6].

Injection Drug Use: Injection drug use has been the principal mode of transmission of HCV since 1970's. In comparison to other viral infections, HCV is more rapidly acquired after initiation of intravenous drug use [7]. In addition, rates of HCV among young injecting drug-users are four times higher than HIV infection [8]. Studies of injection drug users have demonstrated that the prevalence of HCV infection in them is extremely high, with up to 90% having been exposed [9]. In addition, the incidence of new infections is also high, with seroconversion rates of 10-20 percent per year of injecting [10, 11]. Duration of injecting is the strongest single predictor of risk of HCV infection among injection drug users [12].

Sexual Transmission: The topic of sexual transmission of HCV has been controversial. It is believed that HCV can be transmitted sexually, but that it is inefficient -- meaning, it is not easy or likely to pass the virus during sex. On the other hand, HCV infection is very efficient when it is passed from the blood of one person to the blood of another person. The frequency of HCV transmission between monogamous sex partners is very low according to most studies. However, the likelihood of sexual transmission of HCV is increased under any of the following circumstances:

~Having multiple lifetime sex partners
~Engaging in rough sex such as anal sex
~Having a history of a sexually transmitted disease
~Having HIV infection
~Having sex with a prostitute or intravenous drug user
~Having sex during menstruation or whenever blood is present

Other Modes of Transmission: The study of HCV transmission among household contacts is complicated by the difficulty of ruling out other possible modes of acquisition; but overall prevalence of HCV among household contacts of people with HCV is low. "Common sense" precautions such as not sharing items that may have blood on them (e.g., razorblades, toothbrushes) and properly covering open cuts or wounds are advised. Health care workers who have exposure to blood are at risk of infection with HCV and other blood-borne pathogens.

No Identifiable Source of Infection: In summary, individuals can become HCV-infected by sharing needles, syringes or other equipment to inject drugs, or sharing of body fluids with medical injections, or having rough sex with HCV-infected partners. The CDC suggests that transmission can occur through personal items such as razors, nail clippers, toothbrushes, and glucose monitors. Infection can also result from use of non-sterile instruments in health care facilities or other settings, including tattoos and body piercings. Some infants born to infected mothers may get HCV infection via vertical transmission as well. According to the CDC, injection drug use accounts for approximately 60% of all HCV infections in the US, while other known exposures account for 20-30%. Approximately 10% of patients in most epidemiological studies, however, have no identifiable source of infection [13]. HCV exposure in these patients may be from a number of uncommon modes of transmission, including vertical transmission, and parenteral transmission from

medical or dental procedures prior to the availability of HCV testing. It is believed, however, that these are potential modes of HCV acquisition in the setting of inadequate sterilization techniques.

3. ***Diagnosis of HCV.*** Diagnostic tests for hepatitis C include serologic assays that measure human antibodies generated in response to HCV infection and molecular virologic assays that directly detect HCV RNA. Antibodies to HCV can be detected in the blood, usually within two or three months after the virus enters the body. The 3rd generation HCV EIA test is the most frequently used antibody test to initially screen for HCV infection. However, HCV antibody positive simply means that the individuals has exposed to HCV, whether the virus has been spontaneously cleared or persistent in the body need additional test, i.e. looks for the viral genetic material (HCV RNA) that causes hepatitis C. Once confirmed HCV RNA positive, further testing HCV genotype, liver function is necessary in order to proceed antiviral treatment. Notably, the stage of chronic liver disease is graded according the level of liver scarring under a fibrosis score, which is traditionally evaluated by the liver biopsy and now days by the Fibroscan (elastography technology) that can provide data parallel to the biopsy results. A score of F0 or F1 indicates a lack of or minimal scarring, F2 is an intermediate stage of fibrosis, while a score of F3 indicates severe or bridging fibrosis, and stage 4 indicates liver cirrhosis. Some clinicians also calculate *Metavir stage or* Fib-4 score based on patient's age, liver enzymes, and platelet count to determine the severity and stage of liver fibrosis.

4. ***Treatment of HCV.*** Traditional treatments using combination of PEGylated interferon (IFN) and ribavirin (RBV) were often ineffective and accompanied by significant side effects. IFN/RBV treatment lasts 12-48 weeks, has low rate of effectiveness (50% efficacy), and causes debilitating side-effects similar to chemotherapy. Following the foot-steps of HIV therapy, HCV treatment has remarkably improved by developing oral regimens containing direct acting antivirals (DAA) agents. At the initial transition period, however, the HCV treatment was evolved to IFN-based DAA-containing regimen including IFN + RBV + boceprovir or telaprevior. At this short period of transition time, the treatment provided, at best, a 70% cure rate, and was still accompanied by the significant adverse effects such as flu-like symptoms, muscle pain, bone pain, joint pain, nausea, anemia, insomnia, anxiety, depression, memory loss, hair loss, and even death, primarily due to the IFN injection in the regimen. Starting in 2011, the US Food and Administration (FDA) has approved a series of all DAA oral medications for the treatment of chronic hepatitis C. The combination of these DAAs into one pill, once a day, regimen without the IFN injection, lasting 8-12 weeks without harsh side-effects, has resulted in a cure rate of more than 96% with sustained virological response (SVR, defined as HCV RNA remains undetectable 12 weeks after stopping the DAA treatment). Since then, DAA has been recommended by both AASLD and IDSA to become the "standard of care" for patients with chronic hepatitis C. IFN-based treatment is "not recommended" anymore.

III. MORE INFORMATION ABOUT DAA TREATMENT FOR HCV INFECTION

Unlike hepatitis A and B, there is no vaccine currently available for prophylaxis of HCV. However, recent advances in oral DAA treatment have dramatically improved outcomes for patients with HCV [14, 15]. A new concept is thus evolved: Therapy = Prevention (disease progression as well as transmission). These new DAA agents offer a sustained virological response (SVR) (ie, an absence of HCV RNA in the blood at least 12 weeks after treatment completion) or virologic cure in more than 96% of patients [16]. The ability of these agents to cure HCV is critical, as clinical practice guidelines from both the AASLD and the IDSA recommend treating patients to prevent progression of liver disease and reduce the risk of the complications of liver cirrhosis, liver cancer, and all-cause of liver-related mortality.

Currently Available DAA Agents: In 2011, the first DAA agents were approved in the US: the NS3/4A protease inhibitors telaprevir and boceprevir [1, 3]. Although these treatments revolutionized the landscape of HCV treatment with SVR rates ~70%, they could only be used in combination with pegylated IFN and RBV, which are associated with unfavorable side-effects [17]. Additionally, these agents were only effective for patients with HCV genotype 1, leaving few treatment options for patients with HCV genotypes 2 ~ 6. In 2014, the approval of 2 additional NS3/4A protease inhibitors, simeprevir and sofosbuvir, brought the first interferon-free combination therapy to the HCV treatment pipeline [17]. More recently, several NS5A inhibitors, an NS5B nucleotide polymerase inhibitor, and an NS5B non-nucleoside polymerase inhibitor have joined the US FDA-approved HCV armamentarium for use in combination therapies. Table 1 shows currently available DAA agents for HCV treatment in the US [17].

Table 1. FDA-Approved DAA Agents for HCV Treatment

NS3/4A Protease Inhibitors	NS5A Inhibitors	NS5B Nucleos(t)ide Polymerase Inhibitor	NS5B Non-nucleoside Polymerase Inhibitor
Boceprevir	Daclatasvir	Sofosbuvir	Dasabuvir
Glecaprevir	Elbasvir		
Grazoprevir	Ledipasvir		
Paritaprevir	Ombitasvir		
Simeprevir	Pibrentasvir		
Telaprevir	Velpatasvir		
Voxilaprevir			

This surge in DAA options has rapidly changed the landscape of HCV treatment, and two or three agents fused into one pill, once a day, regimen become more popular in the field. These DAAs include Harvoni (ledipasvir/sofosbuvir), Olysio (simeprevior), Sovaldi

(Sofosbuvir), Viekira Pak (ombitasvir/paritaprevir/ritonavir plus dasabuvir), Zepatier (elbasvir/grazoprevir), Eplusa (sofosbuvir/velpastasvir), and most recently approved Vosevi (sofosbuvir/velpatasvir/vovilaprevir) and Marvyret (gelcaprevir/pibrentasvir). In most cases, these agents are approved in specific combinations and should be prescribed based on individual patient- and disease-related factors, such as HCV genotype (1 through 6), the presence or absence of liver cirrhosis, and prior treatment experience [4]. Table 2 shows currently available combination treatments and some of their prescribing uses, as well as the recommended duration of treatment (which may vary due to individual factors, including treatment experience and presence of cirrhosis) [17-19].

Table 2. HCV Treatment Regimens, Indications, and Considerations for Use

Regimen	Genotype	Use in Patients With Cirrhosis	Duration (wk)	Other Considerations
Elbasvir/grazoprevir	1, 4	Not if decompensated	12 to 16	Treatment experienced
Glecaprevir and pibrentasvir*	1-6	Not if decompensated	8 to 16	Treatment experienced
Paritaprevir/ritonavir/ ombitasvir + dasabuvir	1,4	Not if decompensated	12 to 24	Add ribavirin for genotype 1a
Paritaprevir/ritonavir/ ombitasvir + ribavirin	4	Not if decompensated	12	Treatment experienced
Sofosbuvir/daclatasvir	1, 2, 3	Compensated and decompensated	12 to 24	Treatment experienced
Sofosbuvir/ledipasvir	1,4, 5, 6	Compensated and decompensated	8 to 24	Treatment experienced;
Sofosbuvir/simeprevir	1,4	Not if decompensated	12	Treatment experienced
Sofosbuvir/velpatasvir	1-6	Compensated and decompensated	12 to 24	Treatment experienced
Sofosbuvir/velpatasvir/voxilaprevir*	1-6	Not if decompensated	12	Treatment experienced

*Most recently FDA approved, in July or August 2017.
Data derived from Horsley-Silva J, Vargas HE; Vosevi; Mavyret; US FDA [17-26].

Clearly, the HCV armamentarium has expanded rapidly over the past several years, yet there has still been a need for new agents to address specific treatment challenges,

particularly when the first DAA regimen fails. In this exciting time for HCV treatment, new medications are enabling more patients to reach virological cure (SVR) and effectively clear their infection. In conclusion, these novel DAA treatments are effective and well tolerated and can be used to target individual patient needs based on HCV genotype, cirrhosis status, and previous treatment experience.

While being effective and well-tolerated, the cost of these DAA therapies is extremely high at this point (marketing price one pill cost >$1000, 12 week treatment cost nearly $100,000 for medication alone), which has become a major limitation to use for treating most HCV patients who currently needs pre-approval by the insurance companies (it is not ethical to only approve those HCV patients with advanced liver diseases, which is usually too late to prevent serious outcomes, and disapprove majority of HCV patients who usually only have mild liver diseases). It is also the major factor for consideration by most federal agencies and/or state facilities to make decisions about their agenda, policies or criteria to treat individuals with hepatitis C. Notably, the cost of DAA therapy may expect to drop significantly in the near future. For example, Gilead has licensed the same product (Harvoni: sofosbuvir/ledipasvir) to be manufactured in India where only cost < $1,000 for a course of 12 week therapy (that is about 1/100 of US marketing price). Nevertheless, it is clear that these decisions (policies regarding whether HCV patient should be treated and who should be treated first by the effective DAA therapy) were made, not based on the scientific data in the field, but based on financial considerations in most cases.

IV. DAA TREATMENT IS THE STANDARD OF CARE FOR INDIVIDUALS WITH HCV

1. **DAAs are the Standard of Care for HCV Treatment Irrespective of Fibrosis Score:** The leading liver disease and hepatitis C treatment medical organizations, the AASLD and the IDSA, have issued Guidance for Testing, Managing and Treating Hepatitis C. The treatment recommendations in this Guidance are evidence-based, backed by studies and peer-reviewed literatures, and were developed by a panel of HCV experts in the fields of Hepatology and Infectious Diseases. The recommendation are published at http://hcvguidelines.org/full-report-view. Please also see ***Exhibit D***. As set forth in the recommendations, DAAs are the standard of care for the treatment of individuals with chronic HCV infection, regardless of their fibrosis score. The treatment recommendations specifically confirm that DAAs SHOULD NOT be reserved for individuals with advanced liver diseases (fibrosis scores of F3 and F4, and/or accompanied by extrahepatic manifestations). Rather, the standard of care is to treat all patients with chronic HCV infection, except those with short life expectancies who cannot be remediated by DAAs, by transplantation, or by other medical therapy. As the Guidance explains:

"*Initiation DAA therapy in patients with lower-stage fibrosis augments the benefits of SVR. In a long-term follow-up study, 820 patients with Metavir stage F0 or F1 fibrosis confirmed*

by biopsy were followed up for up to 20 years (Jezequel, 2015). The 15-year survival rate was statistically significantly better for those who experienced an SVR than for those whose treatment had failed or for those who remained untreated (93%, 82%, and 88%, respectively; P=.003). The study results argue for consideration of earlier initiation of antiviral treatment. Several modeling studies also suggest a greater mortality benefit if treatment is initiated at fibrosis stages prior to F3 (Zahan, 2015; McCombs, 2015)".

"*Treatment delay may decrease the benefit of SVR. In a report of long-term follow-up in France, 820 patients with biopsy-confirmed Metavir stage F0 or F1 fibrosis were followed up for as long as 20 years (Jezequel, 2015). The authors noted rapid progression of fibrosis in 15% of patients during follow-up, and in patients treated successfully, long-term survival was better. Specifically, at 15 years, survival rate was 92% for those with an SVR versus 82% for treatment failures and 88% for those not treated. In a Danish reginal study, investigators modeled treatment approaches with the aim of evaluating the benefit to the region in terms of reductions in morbidity and mortality and HCV prevalence. Although they note that in their situation of low HCV prevalence (0.4%), with approximately 50% undiagnosed, a policy that restricts treatment to those with Metavir fibrosis stage F3 or higher would decrease mortality from HCC and cirrhosis, the number needed to treat to have the prevalence of the disease is lower if all eligible patients receive treatment at diagnosis. A modeling study based on the Swiss HIV Cohort Study also demonstrated that waiting to treat HCV infection at Metavir fibrosis stages F3 and F4 resulted in 2- and 5-times higher rates of liver-related mortality, respectively, compared with treating at Metavir stage F2* (Zahnd, 2015)".

"*A US VA dataset analysis that used very limited end points of SVR dating from the IFN-treatment era suggested that early… initiation of therapy increased the benefit attained with respect to likelihood of treatment success and mortality reduction and ultimately decreased the number of patients needed to treat to preserve 1 life by almost 50%".*

2. ***There is No Medical Basis to Support Rationing or Prioritizing DAA Treatment.***
When DAAs were first approved, there was a need to get immediate treatment to those in the early-stages of liver disease. This prioritization was not based upon medical necessity or on questions of the effectiveness of the drug for all persons with HCV. As the AASLD explained on November 16, 2015, the practice of delaying treatment until HCV has progressed cannot be justified on any medical basis:

"*Over the past few years, the FDA has approved multiple new treatments for HCV that offer nearly universal cure rates with minimal side effects. It is a remarkable success story for medical science. Unfortunately, many payers – both private and public – are delaying access to new HCV treatments to patients until their disease has progressed and the liver is further damaged.* ***There is no medical evidence to justify that position and much to justify treating all patients. The AASLD and IDSA endorse treating patients with HCV as the standard of care.*** *In the regularly revised HCV Practice Guidance of AASLD*

and IDSA, it is recommended early treatment of chronic HCV infection before the development of severe liver disease and other complications to improve overall survival rates. Studies demonstrate that new treatments cure more than 99 percent of patients followed for five years".

As an infectious disease physician caring HCV patients at daily basis for many years, I concur with these findings and conclusions. With an ample supply of DAAs now available, it is critical for individuals with HCV to be treated before there is damage to the liver or some other extrahepatic manifestations of HCV infection. The current recommendations provided that *"because of the many benefits associated with successful HCV treatment, clinicians should treat HCV-infected patients with antiviral therapy with the goal of achieving an SVR, preferably early in the course of their chronic HCV infection before the development of severe liver disease and other complications".*

3. **HCV treatment that leads to a cure is the only evidence-based intervention to prevent liver disease progression.**
A significant number of persons with chronic HCV who have no or mild fibrosis (commonly described as F0 ~ F1) will progress to cirrhosis in the absence of treatment. Currently, there is no way to predict who in this cohort will develop advanced liver disease. Delaying treatment for patients until they develop advanced liver disease leads to significant suffering, increased risk of liver cirrhosis and liver cancer, need for liver transplantation, and death, thus not cost-effective anyway. Patients who are unable to obtain curative treatment are at high risk for anxiety, illness uncertainty (the inability to determine the meaning of illness-related events), and depression, regardless of fibrosis stages. Patients who are cured of HCV report a significant improvement in their mental well-being and quality of life. As the disease progresses, so does the risk of medical problems, including HCV-associated heart disease, lymphatic cancers, particularly non-Hodgkin Lymphoma, kidney damage, and immune-related rheumatoid diseases. Studies show that HCV infection increases the risk of insulin resistance and diabetes by almost four times. Diabetes also increases the risk of liver cancer in people with HCV infection.

4. **Individuals who are Not Treated Promptly are at Risk.**
Individuals who meet the standards set forth by the AASLD and IDSA, but who are excluded from receiving care, are put a significant risk of many medical complications of HCV infection. HCV is known to have extrahepatic manifestations, described as effects on organ systems outside the liver. Without treatment, individuals may be needlessly exposed to depression, fatigue, sore muscles, joint pain, kidney injury, diabetes or glucose intolerance, certain types of rashes or autoimmune diseases, lymphoma and leukemia. Without treatment, individuals with HCV are at increased risk of developing cirrhosis, liver cancer and liver failure requiring transplant. Furthermore, once individuals develop advanced liver disease, they must undergo cancer screening at regular intervals for the rest of their life even after they are cured of their HCV infection. In addition, the

lack of treatment of infected individuals increases the chance that others will be exposed to, and contract, HCV.

V. DAAs ARE MEDICALLY NECESSARY FOR INDIVIDUALS DIAGNOSED WITH HCV

1. **Treat ALL Patients with Hepatitis C with DAAs is the Standard of Care.**
The guidance issued by the AASLD and IDSA reflect the uniform national standard of care for the treatment of HCV infection. Failure to provide DAAs to individuals with HCV infection when they meet these standards is below the standard of care. Currently, the VA, Medicare, CDC, and a number of state Medicaid systems, provide treatment with DAAs to all patients with chronic HCV infection.

   The AASLD and IDSA Guidance is based on a rating system, a copy of which appears at http://hcvguidelines.org/full-report/methods-table-2-rating-system-used-rate-level-evidence-and-strength-recommendation-each. A statement with the highest rating, Class I, is a "condition for which there is evidence and/or general agreement that a given diagnostic evaluation, procedure, or treatment is beneficial, useful, and effective". Likewise, Class A reflects "data derived from multiple randomized clinical trials, meta-analysis, or equivalent". The recommendation for treatment for all patients with chronic HCV infection, with the exception of those with short life expectations, is at Class I, Level A.

2. **Delayed Treatment Falls Far below the Standard of Care, and is Not Medically Defensible.**
Mere observation and "monitoring" of HCV patients, with no antiviral treatment is medically inappropriate, falls below the standard of care, and risks the health of the individuals with HCV infection. A patient with chronic HCV infection may be outwardly asymptomatic; however, antiviral treatment is nonetheless appropriate. Delaying treatment has a variety of adverse effects including increasing the risk of death, causing irreversible liver damage, and needlessly prolonging suffering associated with the disease. From a public health prospective, observation without treatment risks spreading the disease to others. It is critical that patients with chronic HCV infection be treated before the liver has been seriously and irreversibly damaged by the virus. Delaying treatment while that individual's liver degrades significantly increases the risk of death from cancer, liver failure and a liver transplant. Once a person reaches a fibrosis score of F3, his/her chance of getting liver cancer is so significant that it is recommended that, even after having been cured with a DAA, the individuals undergo twice yearly imaging surveillance for liver cancer.

In addition to liver damage, delay in treatment can cause damage to other vital organs as well. It is systemic disease that, if untreated, can cause heart attacks, fatigue, joint pain, depression, sore muscle, arthritis, and at times, premature death (Hepatitis C virus as a systemic disease: reaching beyond the liver, Hepatology International, 2015, Vol 4, No.4). Therefore, I strongly agree with the current HCV Guidance, which provide that "because of the many benefits associated with successful HCV treatment, clinicians should treat HCV-infected patients with antiviral therapy with the goal of achieving an SVR, preferably early in the course of their chronic HCV infection before the development of severe liver disease and other complications". These benefits include improving or preventing extrahepatic complications, including diabetes mellitus, cardiovascular disease, renal disease, and B-cell non-Hodgkin lymphoma, which are not tied to fibrosis stage of liver.

3. **DAAs are Cost-Effective.**
Treatment of HCV infection with DAAs is cost-effective. There have been a variety of studies examining the cost effectiveness of DAAs to the health care system [27-34]. These studies have concluded that DAAs, although seems "expensive", are actually the same price as the traditional combination treatment for HCV prior to the all oral therapies and are cost-effective to the health care system when the costs of treating advanced liver disease, cancer and associated manifestations of HCV down the road are considered. Indeed, the treatment is most-cost-effective when provided to patients with lower fibrosis scores. Treatment initiation at earlier stages of liver fibrosis resulted in improved health as well as economic outcomes. Thus, DAAs yield more favorable future health and economic outcomes for patients across all levels of treatment experience and cirrhosis stage, as well as individuals with or without HIV coinfection. Given these results, DAAs use should be recommended in every eligible patient awaiting HCV treatment.

4. ***DAAs are Necessary for Public Health.***
DAAs provide an opportunity to eliminate the HCV infection, a goal designed as a priority by the World Health Organization (WHO) at the February 2016 Asian Pacific Association for the Study of the Liver (APASL) meeting in Tokyo, Japan. More recently, the National Academic of Sciences, Engineering and Medicine published a National Strategy for the Elimination of Hepatitis B and C, Phase Two Report in March of 2017, and cited the critical role that prisons must play in achieving the goal of HCV elimination: "The prison population bears a particularly high burden of viral hepatitis, and the criminal justice system should screen, vaccinate, and treat hepatitis B and C in correctional facilities according to national clinical practice guidelines". As HCV survives only in the human body, it is entirely possible that HCV, like polio, can be eliminated. Elimination in only possible, however, if patients get timely treatment in order to stop the spread of the disease. Individuals forced to wait until they have severe fibrosis or full-cirrhosis are at risk of infecting others.

VI. THE TDOC HEPATITIS C PROTOCOL AND THE TDOC PRACTICES AND POLICES FOR THE TREATMENT OF INMATES WITH HCV INFECTION DEPRIVE INMATES OF NECESSARY MEDICAL CARE FOR SERIOUS MEDICAL CONDITIONS

The TDOC, by practice and policy, rations DAA treatment for inmates with HCV infection, which is definitely below the current standard of care, depriving inmates of necessary medical care for serious conditions. Despite knowledge of their HCV infection and the fatal effects of the disease, the TDOC has consistently and systemically denied inmates effective treatment, although the department has committed to offering quality health care to inmates that meets "the community standard of care". There is agreement among medical professionals and organizations responsible for the development of community standards for treatment of hepatitis C, including the leading medical organization on this issue and the established practices of VA, Medicare, Medicaid, the CDC, and other providers of medical care, that DAA should be provided to all persons with chronic hepatitis C, subject to certain limitations not related to the stage of the disease. The TDOC, however, currently only provides DAA to a very small number of inmates with HCV infection and continues to deny DAA treatment to thousands of other HCV-infected inmates. According to the supplemental interrogatory response by Dr. Williams, who developed the HCV policy (or guidance), chairs the TACHH Committee since 2012, and serves as the final policymaker with respect to treatment decisions regarding HCV-infected inmate-patients, all decisions made relating to the administration of pharmaceutical regimens for the treatment of chronic hepatitis C (cHCV) infection in inmate-patients have been made by the TACHH Committee on a case-by-case basis. As a matter of fact, till May 2016, only 8 of the 3,487 diagnosed HCV inmates in TDOC system were receiving treatment with DAA (25 over the last 12 month, Dr. Williams DEP P122). Furthermore, some written polices for HCV diagnosis, assessment and treatment utilize outdated standards of care and normalize the practice of refusing treatment for medically unsound reasons. The protocol specifically omitted DAA treatment, but contemplates use of IFN/RBV (As documented on Page 11-15 of 24: current treatment include a medication that may be injected every week for up to 48 weeks; initial side effects may include flu-like symptoms; treatment will continue to evolve in the next a few years as experts develop new medications that will work even better and well-tolerated by the patient), even though those drugs are widely considered "inferior" and are disfavored for treatment of HCV. As explained below, the reasons provided by the TDOC for rationing or prioritizing DAA treatment are without a reasonable medical foundation.

A. The TDOC Hepatitis C Protocol

1. The provisions of the Protocol, attached as **Exhibit C**, regarding Screening Criteria, Risk Factors, and Recommended Testing (Page 4 of 24) are seemingly

adequate as written. In March 2016, the TDOC placed the number of its inmates testing positive for HCV at 3,948, by July 2017 over 4,000 (per DEP by Tony Parker), or nearly 1 in 6 prisoners (>15% HCV+ in ~20,000 inmates currently in TDOC custody), while conceding that this number is likely far below true infection rates due to a lack of routine testing and inaccurate testing. The protocol establishes a convoluted, multi-step assessment procedure between the diagnosis and the treatment lasting an unreasonable long time (Page 18-20). According to the supplemental interrogatory response by Dr. Williams, the inmate-patients enrolled in the chronic care clinic are scheduled to be seen by a physician or clinical nurse every 6-12 months. In practice, that waiting time is greatly extended by delays in making appointment, receiving the results of test, etc.

2. The Protocol's policies for Assessing Hepatic Cirrhosis and Decompensation (Page 5 of 24) and for determining the metavir fibrosis stage for inmates with HCV infection are deficient and cause denial of DAA treatment even to those HCV-infected inmates who the TDOC, by policy and practice, have prioritized for DAA treatment. Currently, medical professionals use two types of tests to determine the advancement stage of HCV, by fibrosis and cirrhosis stage. Blood tests can provide an "APRI (AST Platelet Ratio Index) score", determined from a ratio derived from the level of an enzyme in the blood AST compared to AST levels of healthy persons and the number of platelets in the infected person's blood (APRI = AST/AST ULN x 100 / Platelet count x 10^3/µl / 1000). The APRI score provides useful, but often imprecise measures of fibrosis or cirrhosis (sensitivity only 37-48%, and specificity of 75-94%). A very high APRI score provides a reliable diagnostic measure of severe fibrosis or cirrhosis. For example, in 90% of the cases an APRI score of at least 2.0 reliable shows cirrhosis, but more than one-half of all persons with cirrhosis will have APRI scores of less than 2.0. As the Protocol indicated: "lower APRI scores have different sensitivities and specificities for fibrosis and cirrhosis". In other words, the TDOC Protocol relies entirely on assessment by APRI score, which is an inferior means of measuring fibrosis staging because it results in under-detection of cirrhosis.

   The best test for measuring the advanced stage is the FibroScan, a type of ultrasound known as "transient elastography" that images the liver tissue and provides a measure of fibrosis or cirrhosis. The FibroScan is the current gold standard in diagnosis as it avoids the complications and dangers of liver biopsy and is far more precise than the APRI score. The Protocol does not mention about the TDOC policies governing elastography machine, limiting their ability using FibroScan to assessing inmates with HCV infection (I even doubted whether the TDOC has this machine by just reviewing their guidelines until I saw the supplemental interrogatory response by Dr. Williams that "in late 2017, TDOC acquired a Fibroscan unit in order to permit TDOC to evaluate the medical condition of cHCV-infected inmate-patients with greater accuracy in a non-invasive

manner. At the time of this supplemental response, training is in progress regarding the use of the Fibroscan equipment to strengthen TDOC's approach to the diagnosis, care, and treatment of cHCV-infected inmate-patients"). Notably, there are portable elastography machines that could be used state-wide to reliably measure the fibrosis/cirrhosis stage of all inmates with HCV infection.

3. The Protocol (Page 9 of 24) provides for additional screening and testing of those determined to have cirrhosis (for example, assessing hepatic compensation, detecting esophageal varices, and screening for HCC). I agree with these provisions, but point out that the positive rates for these tests and screenings would become significantly decreased if individuals were treated early enough to avoid the development of advanced liver disease. With universal treatment, inmates with HCV infection would not advance to the cirrhosis stage and would not present with these dangerous conditions. On the other hand, denying treatment with DAA creates the risk of an HCV transmission among the general population, as HCV positive inmates will be released into the broader Tennessee Community and will likely infect others.

4. The TDOC Criteria for HCV Treatment (Page 10 of 24) reflects the current TDOC rationing and prioritization process (Level 1-4). Likewise, according to the comments per Supplemental Interrogatory Response by Dr. Williams, "Inmate-patients with fibrosis scores of F0, F1, and F2 are not at need of treatment with currently-available DAAs…Due to the uncertainty relating to the efficacy of currently-available DAA regimens, as well as the potential for yet-unknown side effects from the administration of DAAs, the TDOC and its healthcare providers consider that expenditure of resources for the treatment of cHCV should be modulated… - until greater certainty concerning the efficacy of available DAA regimens is scientifically demonstrated"; "cHCV-infected individuals who do not experience significant complications or an accelerated level of viral progression continue to receive routine and consistent monitoring of their condition until such time as they reach a classification warranting the administration of the pharmaceutical regimen." In my opinion, there are serious medical flaws in both these diagnostic and treatment regimens. First, as explained above, there is no medical justification for prioritization of antiviral treatment. TDOC's rationing by priority level is, to many medical professionals, clearly medically flawed and below the standard of care recommended by AASLD/IDSA. Second, even if priorities were acceptable, F-score is based primarily on the APRI calculation and very few inmates are provided a FibroScan that is still unavailable in the TDOC system. Thus, the initial determination of the fibrosis-score is highly unreliable. Third, even where all diagnostics point to cirrhosis or advanced fibrosis, there is no provision in the policy that mandates DAA treatment; rather, other evaluations are required (which recognizes the benefit of universal treatment, but then prioritizes DAA treatment according to APRI scores). To date, >15% of all inmates are found with

HCV infection, but there is only a few of them received DAA treatment (25 over the last 12 month, Dr. Williams DEP P122). Thus, there are thousands of patients with a serious medical condition that will worsen over time and some of who have already manifested symptoms, who are denied a medical treatment that would fully cure them of this illness. In fact, according to the supplemental interrogatory response by Dr. Williams, prior to fiscal year 2015-2016, no patient-inmates were treated with DAA in TDOC system, although multiple DAAs had been approved by FDA and recommended by AASLD/IDSA several years ago. Indeed, the complicated and costly, but ultimately unreliable diagnostic and treatment standards in the Protocol would be entirely unnecessary with universal treatment ("Universal treatment" means no restrictions by fibrosis score. There are only a few restrictions related to medical issues may justify no DAA treatment, for example, for those who have very short life expectancy).

Also, it is important to note that the DOC does not appear to follow its own staging Protocol. The medical records of Plaintiff Russell Davis indicate that he is at F4 cirrhosis of the liver discovered through liver biopsy (Clinical Summary date 5/19/2017 discussing biopsy results, Page 55 of his record notes F4 score); however, despite his advanced staging and expressed symptoms such as pain and leg swelling he has been denied DAA treatment by the TACHH Committee.

5. The protocol places unnecessary restriction on DAA treatment, despite TDOC's awareness of AASLD/IDSA guidelines and acknowledgement of Federal Bureau of Prisons (FBOP)'s current policy to screen all inmates for HCV infection and treat them with DAAs (See Management Guidance at p.8). Inmates can be denied DAA treatment for multiple reasons, for example, if they have less than 9-12 months (Page 11 and 20) remaining on their sentence in the TDOC to complete a course of treatment (even though the course of treatment is only 8 or 12 weeks); or have documented positive drug screens or non-adherence with other medical regimens previously. An inmate who has been disciplined also becomes ineligible to the treatment, so does an inmate who has received a tattoo within the last year, who has used drugs or non-prescribed medications or alcohol in the last year, or who generally considered by the DOC a behavioral risk. Inmates who are not capable of giving or understanding the multiple pages of informed consent, and those with certain mental illness or solid organ transplant recipient, will also be denied treatment. Necessary medical care should not be denied based on possible non-compliance with best health practices. Also, the protocol listed special contraindications to limit the use of DAAs, for example, GFR has to > 30 (which ignores the fact that several DAA regimens are FDA approved for HCV patients with renal deficiency, another point reflecting their out of date Protocol).

6. Doubtless many inmates have died from liver related diseases and other conditions most likely caused by HCV infection while in TDOC custody since 2010.

One medical provider admitted he was aware of one such death (Dietz DEP P47), and news articles note other such deaths (As reported - https://www.tennessean.com/story/news/local/2016/07/01/tennessee-inmate-asking-hepatitis-c-treatment-dies/86611846/ - John Bilby knew he didn't have much time left. But, at least for a few days, it appeared as though the longtime Tennessee inmate and sufferer of hepatitis C might have some hope. Diane Douglas, Bilby's wife, said he was recently told he was at the top of the list to receive the best available treatment for his hepatitis C, a chronic disease that slowly destroys the liver. Douglas said the day after Bilby told her this, he died), though Williams has commented that "In my capacity as TDOC Chief Medical Officer and Director of Medical Services, I have no knowledge that inmates have died while in the custody of TDOC of complications arising from cHCV-infection since 2012". Pending further discovery in this case, I reserve the right to provide a further opinion on whether these patients would have survived if they had been treated with DAA.

B. Current Practices beyond the Protocol

1. The TDOC says it has a policy of providing medical treatment under community medical standards. As written by Derrick D Schofield (Commissioner) in his response to questions raised during the hearing to Charles M. Sargent (Chairman): Currently, TDOC offers the most up-to-date treatment available for hepatitis C (**Exhibit B**). Thus, the contract between the TDOC and the medical provider (Medical Service contract with Centurion, CoreCivic facilities), refer to Health Care Solutions, mandates medical care under community standard and inmates are informed of these community standards in the grievance process (see Dr. Williams Dep. At p31). Yet, the TDOC fails to follow clearly established community standards for the treatment of hepatitis C, and fails to provide any medically relevant reason for not providing DAA treatment to all inmates with HCV infection. The TDOC does not deny that the standards for treatment of HCV in the community is set forth by AASLD and other leading medical organizations and programs: DAA treatment for all, without rationing or prioritization, with the exception of a very limited number for reasons of lack of efficacy of the DAA for their condition or very short life expectancy. In practice, the TDOC MD provider fails to follow the established community standards of care for individuals with hepatitis C. I even question whether the providers have the appropriate training or understand the nature of chronicity of HCV infection. For example:

    a. Depo of Dr. Kavin Johnson, he mentioned the inmates are followed every 3 month for chronic care, if an inmate's APRI score is less than 2, then he will treat the inmate's other conditions "to give the liver a chance to clear the virus…page 55…15 to 20 percent of hepatitis C patients – their body will remove the virus on their own with no treatment" (Bear in mind that he is talking about chronic hepatitis C, not acute Hep C that can spontaneously

resolve the infection). (Page 56, Q: And so if I understand you correctly, you would continue monitoring inmates whose APRI score is less than 2 while they are in chronic care in hopes that they might fall into that 15 to 20 percent of folks who clear the virus, is that correct? A: That's correct). Then on Page 82-83, (Q: Do you know how long it typically takes someone to clear the virus, those 15 to 20 percent, like you just mentioned? A: It could take – it is very variable. It could take six months. It could take six years. It could take 16 years). Apparently, this medical provider does not understand the nature of HCV infection. How this MD provider be expected to follow the community standard of care for inmates with hepatitis C in practice competently without an adequate policy?

b. Depo of Dr. Bernhard Dietz, he also mentioned that in his prison clinic he sees inmate-patients with chronic HCV infection for more than a year who clear the virus "very often," "a few times a month, maybe. Several." (Page 81). Of course, this is not possible, which begs the same question as above.

2. The administrative burdens of following the TDOC Guidance are far than following the current medical standards for treatment. The TDOC cites the need for medical testing and diagnosis to determine Fibrosis score, genotype, possible medical contraindications to DAA treatment (e.g., co-morbidity), movement and transportation of inmates for some testing purposes, and establishment of medication regimens. But almost all of these supposed administrative hurdles are the function of a system that rations and prioritizes treatment. In a system of universal DAA treatment, the current protocols for screening all new inmates for HCV along with readily available inmate medical records reflecting any other relevant medical conditions, all that must be done before DAA treatment is started is the identification of the genotypes (already in the database), possible contraindications to treatment given other medical conditions or life expectancy, informed consent, and the start of a simple, one pill a day regimen, with limited monitoring needed over the 8-12 week period of medication. If there is no prioritization, there are none of the administrative burdens, including multiple medical tests associated with monitoring of inmates.

3. Indeed, to the extent that any testing is necessary, elastography can provide virtually all the information necessary as to fibrosis advancement. If the TDOC is accurate in stating that all persons at F3 and F4 are currently being treated, those at F0 to F2 will rarely present any medical or administrative problem that would prevent treatment of the entire backlog class of inmates. Thereafter, as new inmates come into the system, they could be treated within months or even weeks of their initial screening.

4. Moreover, any claim of administrative or security barriers to treatment of all HCV inmates with DAA would be highly suspect given the fact that in the extensive documentation of efforts by the DOC to develop the Protocol and establish standards and procedures for DAA treatment, there is not a single document that cites administrative or security reasons for not providing universal treatment. To the contrary, the other documents address financial costs, available resources, and make no mention of other barriers.

5. Finally, the administrative burdens, even if they were real, are largely a function of finances, in terms of the personnel and testing equipment necessary to operate a system that rations or prioritizes treatment. And this leads into the likely reason DOC does not following current medical standards – the financial costs of the DAA[1]. While the TDOC has maintained that it is the disease progressions and not financial burdens that the driving force behind prioritization, even if costs are significant, community standards are reflected in national guidelines and actual practices of leading organizations and medical programs. Many insurers have voluntarily removed similar restrictions on the available of HCV DAA treatment, such as BlueCross, Atena, United Healthcare, Medicare, Medicaid, VA, CDC, and virtually all private practitioners, mandate universal DAA treatment. Other insurers, Bridgespan, Regency BlueSheld, and Group Health Cooperative, changed their policies within weeks after lawsuits were filed against them on similar grounds to those brought in the above-captioned matter.

In summary, since the chronic hepatitis C disease is serious and progressive at even its early stages and treatment provides a cure with minimum side effects, and reduces costs of monitoring and treatment of others who will not become infected by those treated with DAA, in my opinion, a protocol could be developed that continues to treat the most serious cases immediately, and that ensure universal treatment of all HCV inmates within a designated period of time.

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[1] DOC's medical providers have clearly stated that cost is the reason for DOC's staged treatment protocol. "Q. Can you tell me what, in your opinion, the purpose of the TACHH committee is? A. I believe – well, you want the honest answer? The purpose of the TACHH committee is to spread liability – to spread liability." (Ivens DEP P 50-51). "Q. Are there reasons for not treating everyone with chronic hepatitis C with DAAs? A. Yes. Q. What are those reasons? A. Cost, side effects, difficulty of getting – of making the medication available." (Dietz DEP P 50).

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